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Upper airway in obstructive sleep apnea – controversies continue

The exact pathophysiology leading to pharyngeal collapse in obstructive sleep apnea (OSA) remains incompletely understood. Recent research have focused on the neurochemical and physiological changes occurring at sleep onset that lead to the loss of muscle activity and diminished reflex pharyngeal control, and a loss of the neuromuscular compensation present during wakefulness, resulting in pharyngeal collapse. Regardless of this physiological arm, it is well documented that patients with OSA suffer from compromised upper airway anatomy. Most studies, using a variety of imaging techniques (CT, MRI, acoustic reflection, cephalometrics), have demonstrated a small pharyngeal airway in apnea patients, with the smallest airway luminal size generally occurring at the level of the velopharynx (behind the soft palate) in both patients and controls (Schwab *et al*., 1993). The finding of Walsh *et al*. (2008) from the current issue of the JSR supports these findings as well. Utilizing the novel technology of anatomical optical coherence tomography, they showed that the smallest cross-sectional area in 30 patients with OSA and 10 controls is located at the velopharyngeal level. However, they could not corroborate two previous anatomical findings reported in OSA: the role of airway shape and airway length.

Several previous studies have reported an oval shape of the pharyngeal airway in individuals with OSA when compared with controls (i.e. a relatively high anteroposterior/lateral luminal airway dimension). Furthermore, Leiter (1996) have also suggested a reduced ability of muscles to dilate the pharynx when it is oval in shape. The study by Walsh *et al.* could not demonstrate differences in the AP/lateral diameter ratio between patients and controls. The importance of airway shape was also found to be less significant in a recent study examining the potential mechanisms contributing to increase in the prevalence of OSA with increasing age. Malhotra *et al*. (2006) reported that the ratio of the anteroposterior to lateral dimension became progressively lower with increasing age. Thus, the importance of the oval airway shape as an anatomical predisposing factor in the pathophysiology of OSA remains controversial and unclear.

The length of the pharyngeal airway has received only minimal attention so far. It was previously reported that upper airway length (UAL) was greater in normal men compared with women, suggesting that it may play a role in the male predisposition to pharyngeal collapse (Malhotra *et al*., 2002). Furthermore, using computational modeling, a major impact of UAL on pharyngeal mechanics has been demonstrated (Malhotra *et al*., 2002). In another recent study of 69 healthy boys and girls who had undergone CT scans of the neck, it has been found that the UAL in prepubertal children is equal between genders. However, following puberty, males were found to have longer upper airways than females (independent of systemic growth), thus potentially explaining why pharyngeal collapse has a strong male predominance in adults but not in children (Ronen *et al*., 2007). In addition, a longer pharyngeal airway has been shown in postmenopausal as compared with premenopausal women (Malhotra *et al*., 2006). Thus, the existing data suggest that UAL may at least partially explain the male predisposition to airway collapse that occurs at puberty, and the female predisposition that occurs at menopause. Moreover, data from our own laboratory shows that UAL is greater in patients with OSA than in controls, with a positive significant correlation between the UAL and the severity of OSA (paper under consideration for publication). At least three potential reasons can explain the discrepancy between these previous findings and the findings of the current study by Walsh *et al*.: methodological differences, statistical limitations, and the patient population studied. While previous studies of UAL were based on MRI or CT scans, the current study utilized a relatively novel technology. The anatomical optical coherence tomography is an endoscopic technique, based on infrared light from an optical probe sliding within a preinserted esophageal catheter. While a CT scan is completed within seconds, this technique takes between 9–12 min (for each pullback scan), and may be affected by swallows, head or tongue movements, and by the topical anesthesia applied prior to catheter insertion. In addition, UAL in the Walsh study was determined as the summation of the velopharyngeal, oropharyngeal, and hypopharyngeal segments, thus extending all the way to below the epiglottis, differently from the previous definition for UAL length (between the rigid bony structures of the airway: hard palate to epiglottis). Also, lack of differences in UAL between OSA and controls is based on only 10 subjects in each group, all of whom are men, while the previous studies reporting the importance for UAL had a substantial gender-related effect and were based on substantially larger groups of subjects (Malhotra *et al*., 2002, 2006; Ronen *et al*., 2007). Thus, further studies are required to better understand the role of UAL in obstructive sleep apnea syndrome.

Controversies in OSA are further exemplified in the discrepancy between the anatomical findings and therapeutic results. While Walsh *et al.* as well as Schwab *et al.* (1993) and others have demonstrated that the narrowest and most vulnerable to collapse region of the upper airway is the velopharyngeal segment, the study by Petri *et al.* (2008) also from this issue of the JSR, further supports the therapeutic role of mandibular advancement splints, although these predominantly affect the oropharyngeal and less the velopharyngeal region. In a well-designed placebo-controlled study, they showed that mandibular advancement appliance was beneficial in 27 patients with OSA compared to 25 patients with placebo (mandibular non-advancement device) and 29 untreated patients. They showed that during a period of 4 weeks, the appliance resulted in improvement in apnea hypopnea index (AHI), reduction in subjective sleepiness (Epworth sleepiness scale), and improvement in vitality (SF-36). Moreover, while traditionally mandibular advancement appliances were considered beneficial for only mild-to-moderate OSA, the study of Petri *et al.* shows that at least four patients with severe OSA were completely cured with the device, reaching an AHI of less than 5/h. These results are in agreement with a recent long-term dental device study that reported on an overall reduction of 33% in AHI during a 1-year treatment with the Herbst device (Itzhaki *et al.*, 2007). Some of the patients in that study also had a severe form of OSA. Furthermore, even with a modest improvement, that study showed that the endothelial function improved with the mandibular advancement appliance, suggesting that even with some extent of residual apnea, the risk of cardiovascular complications may be reduced. Thus, the study of Petri *et al.* with strengths in good methodological design, sham treatment control, large patient group with representation of a wide range of OSA severity, is congruent with the accumulating data supporting the concept that mandibular advancement may be a realistic alternative treatment to continuous positive airway pressure in patients with OSA.

In conclusion, the present papers demonstrate that we are still far away from understanding the exact role of the upper airway in the pathophysiology of OSA. Further studies combining advanced diagnostic technologies and individually tailored treatment are required to learn about the role of the various aspects of the upper airway in the pathophysiology of OSA and about the long-term effects and potential side effects of mandibular advancement appliances.

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